

* Denotes the repeating stereochemical triad

FIG. 3

2/48

PMBO
$$N$$
 OMe N DDQ, CH_2Cl_2 (76%) Common Precursor $(+)-5$

Ph₃P=CBrCO₂ Et, PhH,
$$\Delta$$
 PMBO $\stackrel{\stackrel{?}{=}}{}$ Br DIBAL, CH₂Cl₂ PMBO $\stackrel{\stackrel{?}{=}}{}$ $\stackrel{(85\%)}{07BS}$ $(-)-19$ $(-)-20$ $(-)-20$ $(-)-20$ $(-)-20$ $(-)-20$ $(-)-20$ $(-)-20$

3/48

Ю

Mscl, NEt₃

$$CH_2 Cl_2 (99\%)$$

$$CH_2 Cl_2 (99\%)$$

$$0 TBS$$

$$(-)-21$$

(91%)

(+)-18

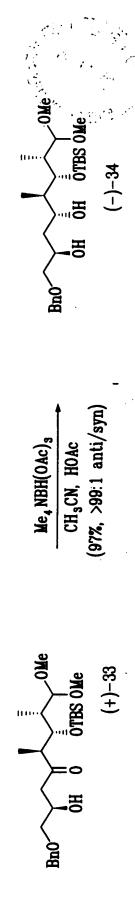
DDQ (1.0 equiv)

CH₂Cl₂, H₂O

FIG. 5

FIG. 6

APPROVED O.G. FIG. BY CLASS SUBCLASS DRAFTSMAN 549 22	0HC
Book regal 200 to Assessment	SO ₃ • py Et ₃ N DMSO (98%)
	FIG. 7 HO TBS $(+)-26$ $(+)-26$
	H ₂ Pd(0H) ₂ /C EtOH (92%)
	PMB0 N OMe OTBS 0 OTBS 0



 $(-)^{-32}$

TBS0,	36 OMe
	2,6-Lut, CH ₂ Cl ₂ (98%)
TBSO	$(87\%, 2.1 \ \beta/\alpha)$ 35 OMe
FIG. 8	OH OH OTBS OME (-)-34
	TBSO,

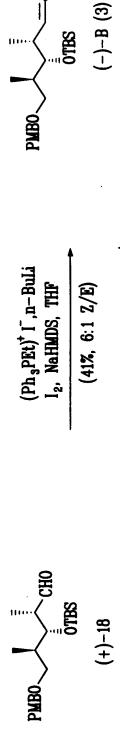


FIG. 10

a) t-Buli (3 equivalent equivalent by
$$(-)$$
-A

Et 20

-78 °C \rightarrow R

b) (-)-B, Pd(PPI

C) Separate Z at

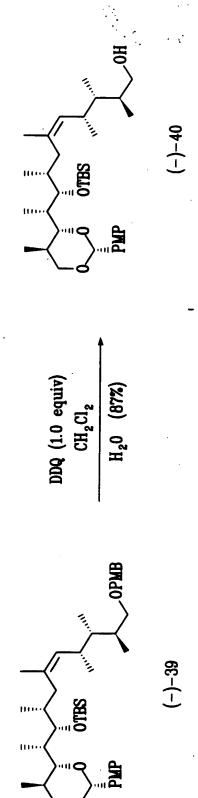


FIG.	SUBCLASS	1292
0.6	CLASS	249
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Imid., PhH/Et₂0 (1:2)

OTBS

	SUBCLASS	7
.G. FIG.	SUBC	77
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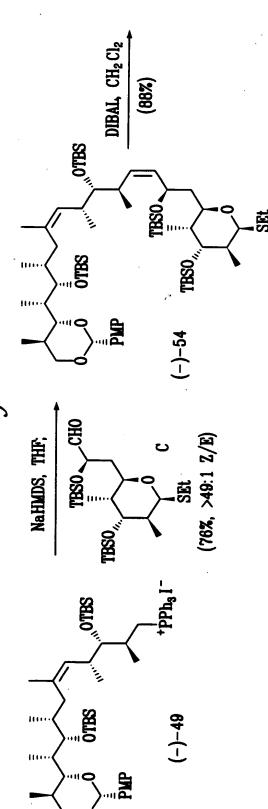
(-)-47

OTBS

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F.	



$$SO_3 \cdot Py$$
, Et_3N , $DMSO$

$$CH_2Cl_2 (96Z)$$

$$(-)-56$$

$$TBSO_{10}$$

$$TBSO_{10}$$

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SUBCLASS 292

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APPROVED O.G. FIG.

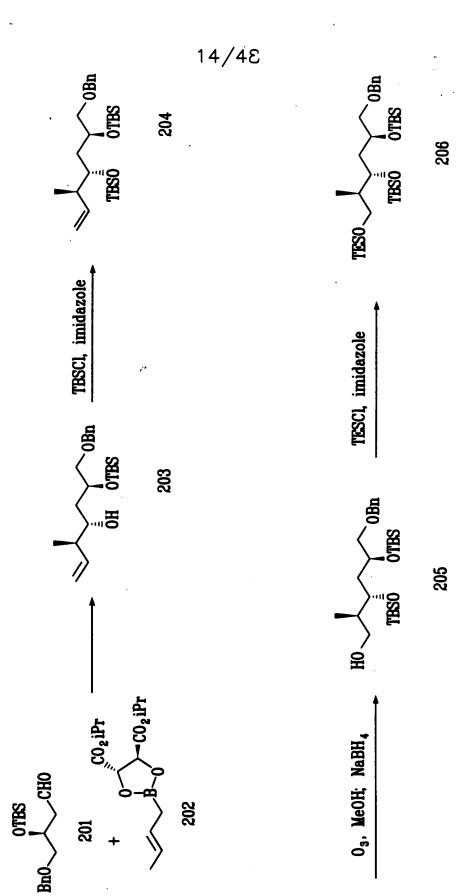
PMBO OTBS	THF TBS0 (-) -58 (-) -58	48	(1: 9) (-)-Discodermolide (1)	
The state of the s	TBS0,	OTBS OTBS	TBSO, (60%) (60%) (1:9)	0 09
FIG. 15	Ph ₂ PCH ₂ CH=CH ₂ t-Buli, Ti(0-i-Pr), Mel, THF (70%, 16:1 Z/E) (-)-57	N ₂ H SaTo	TBS0 (a) Cl ₃ CONCO (CH ₂ Cl ₂ b) Neutral Al ₂ O ₃ (83%)	09-(-)
OHC BARBO OTBS	TBS0,	OH OTBS	DDQ, CH ₂ Cl ₂ , H ₂ O (95%) TBSO,	69-(-)

SUBCLASS 292

OTBS	12/	48	
	TBSO	OTBS	
OTBS	TBS0	OTTES	TBSO
PMBO	illu Culti	PMBO	TB 104
OTBS	Pheculi		
	TBSO	DMSO, Ac20	-
OTBS	TBS0	OTBS	
bl/B0	TsCl, pyridine	\ /	HO HO
FIG. 16 Tso.	Tsci	OTES	TBS0
FIG.	TBSO, OSPH	PMB0	103
OTES	08	(<u>)</u>	į
DIMBO	TT (+)	HgCl ₂	
НО		·	

FIG. 17	Cl ₃ CCONCO, CH ₂ Cl ₂ ; Alumina	13/48	HO
HO OTBS		001 00H0 00H0	NH ₂ NH ₂ HO_
OTTBS	TBSO	104 III O OTBS	TBSO,
PMBO			·

O.G. FIG.	CLASS SUBCLASS	549 293
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		NAME OF THE PARTY



O.G. FIG.	CLASS SUBCLASS	243 Phs
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FIG. 19	OTBS DMS0 208 TBS0 OTBS	HO PMBO OTBS	TBSO,	Ph ₂ PCH ₂ CH=CH ₂ , tBulia PMB0 OTBS	
	TESO TESO OTBS Hz, Pd/C TESO TESO TESO TESO TESO TESO TESO TESO	OTBS	Nathados, The Teso	OTBS	TESO TESO OTES

APPROVED O.G. FIG. BY CLASS SUBCLASS DRAFTSMAN SY? 292		PMB0 OTBS OTBS	(CF ₃ CH ₂ 0) ₂ P(0)CHCO ₂ Et TBSO ₂ TBSO ₂	214 OTBS CO ₂ Et	HO OHO	HO, HO, O
	FIG. 20	OTBS	TBSO	OHC	OTBS OTBS	TBSO, Mecn Mecn Mecn Mecn TBSO, OTBS
		OTTBS PMB0	TBSO, DMSO	Sarro	SETTO	TBSO, CI3CCONCO, CH2CI2, Alumina CO2Et
		PMB0 OTBS		212 212	HO OTBS	DDQ CH2Cl2-H2O

APPROVED O.G. FIG.

BY CLASS SUBCLASS

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	TsO PMBO OTES	TBS0, TBS0, TBS0, TBS0, TBS0, TBS0, TBS0, TBS0	/48 SHLO SHLO	TBSO	HO HO
FIG. 21	OTTES	TBS0, TSC1, pyridine	DAMBO	HgCl2, MeCN	302
	OTES HO F	TBSO, nBuli	PMB0 OTBS	TBSO	304 § SPh
	H PMB0 OTBS	TBS0		LiEt, BH	

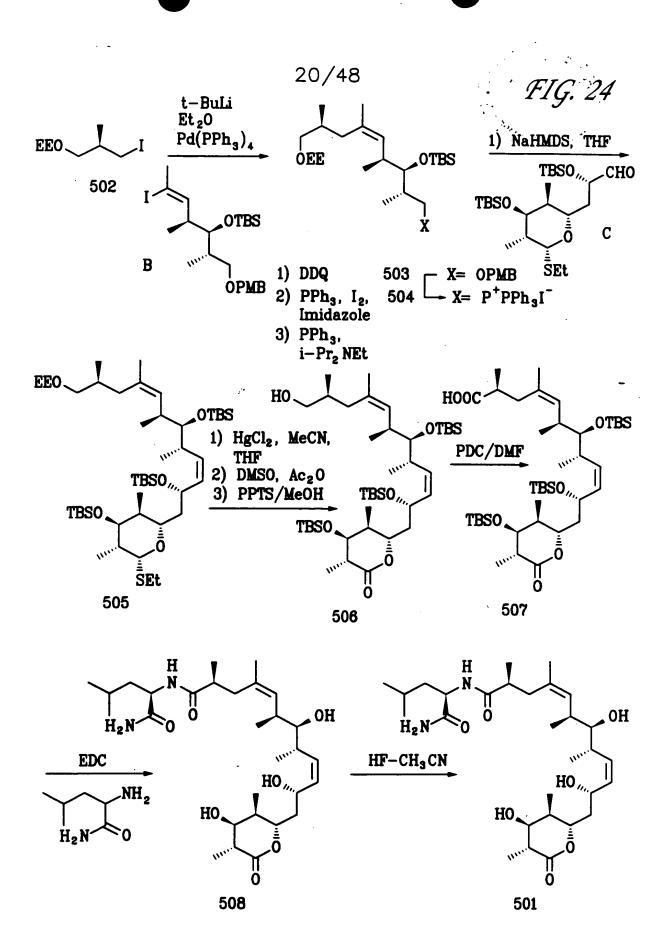
APPROVED O.G. FIG.

BY OLASS SUBCLASS

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	OTBS		18/48	•	
		TBSO	0	OH OH OH	5
	HO OTBS	12-H ₂ 0	307	HO HO	
	OTES	DDQ, CH2Cl2-H20		NHA O	
22	<u> </u>	TBSO	"O O	Q HF/Mecn	-
FIG. 22	PMB0 OTBS	20 TBSO	30e	OTBS	
	OTTES P	DMSO, Ac20		OTBS TBSO	,
		TBS0		308 NH ₂	
	PMB0 OTTBS	TBSO	305	Cl ₃ CCONCO, CH ₂ Cl ₂ : Alumina	
	Ad No.		·	Cl _s CCOM Alu	

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22/48 FIG. 26 R_2CuLi DIBAL -H Et₂O CH₂Cl₂ **OTBS OTBS** Ρ̈́MΒ . PMB A 702 PPh₃ PPh₃ I2 PhH **Imidazole** reflux OH OPMB OTBS OPMB OTBS 703 704 1) BuLi 2) 706 Ph3P+1 OPMB OTBS OPMB **ŌTBS** CHO 705 707 OH oTs TsCl Pyr. Ch₂Cl₂ .0H HO. 80% AcOH room temp. **OPMBOTBS OPMBOTBS** 708 709 K₂CO₃ MeOH DDQ Ch₂Cl₂-H₂O **OPMBOTBS** ŌН ŌTBS 710 711 Cl₃CCONCO (ClCH₂)₂, K₂CO₃ HF / CH₃CN **MeOH** OTBS H₂N ŌН H₂N 0 0 712 701

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25/48 FIG. 29 **ŌTBS** OTBS OTBS OH OPMB OTBS 1) NaHMDS, THF **PMP** 111 903 **OTBS** 15 PPh; I-TBS0 902 EEO **CHO EEO** 2) DIBAL, CH₂Cl₂ **ÖPMB ÖTBS** OTBS 1) SO₃.pyr, DMSO, Et₃N 1) PPTS/MeOH 2) Ph₂PCH₂CH=CH₂ (904) 2) glycosyl bromide (906) t-BuLi, Ti(0-iPr)₄, Mel HgBr₂, CH₂Cl₂ **TBSO** 905 EEO 1) DDQ, CH2Cl2 **OPMB OTBS** OTBS 2) Cl₃CCONCO (CH₂Cl)₂, K₂CO₃ MeOH TBSO, 908 3) 48% HF/MeCN ОМе MeO-MeO 0Me ŌН OH ОМе Br MeO-0Me 901 Me0 HO, 906 ОМе Me0

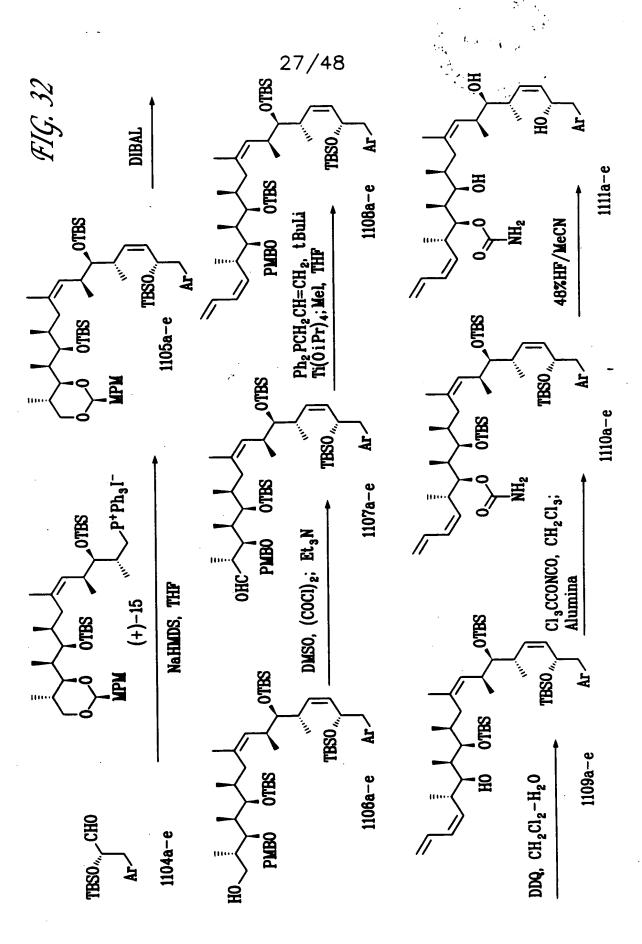
0Me

Me0

APPROVED O.G. FIG.
BY CLASS SUBC

			•	
HO,	26/48 = 0 \$ \$001	OBn SMe ₂	TBSO	Ar 1104a-e
TBSO, TBSO, HO.	= 0	1) On OBn CuBr-SMe2	DMSO, (COCI)2; Et3N	_
otbs $ \begin{array}{c} \text{II. HgCl}_{z} \\ \text{2. DMSO, Ac}_{z} \end{array} $	1002 FIG. 31	Ar ₂ Culi	TBSO,,,	Ar / 1103a-e
TBSO, CHO TBSO, CHO TBSO, THF TBSO, CHO TBSO, TBSO, CHO	1001 SEt	2 eq t-Buli, -78 °C; Cul, ether, 0 °C	H ₂ , Pd/C	
NaHMDS, THF OTBS TBSO TBSO TBSO TBSO TBSO TBSO TBSO		Ar-Br 2 .	TBSO,,,	Ar / 1102a-e

J.G. FIG.	CLASS SUBCLASS	549 245
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SUBCLASS
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NH2	29/48 HO OH OH OH	HO HO HO
NH ₂ HO, OH	HO HO OH	HO H
	HO HO HO	HO OF OF
OH OH OH OH	0 HO HO HO	NH ₂ HO OH

APPROVED O.G. FIG. BY CLASS SUBCLASS DRAFTSMAN S49 29 2		HO, HO, I	30/48 HO HO H	HO HO OH
	FIG. 35	HO OHO	HO	OH S HO, HO, HO,
		OH OOH OOH	OH OHO OHO OHO	OME OOH NH ₂ HO O
		HO OH NHR ₂	O OH OHO OH	HO, HO, OH

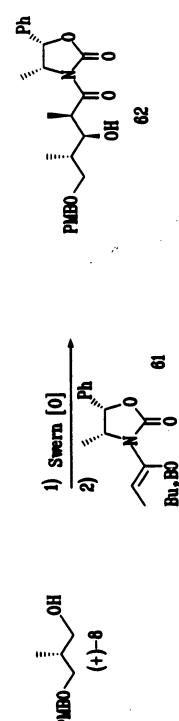
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$$H_2N$$
 O
 OH
 OH
 OH
 OH

- <u>i</u> G.	SUBCLASS	267
O.G. FIG	CLASS	648
APPROVED	À	DRAFTSMAN

aezange, engene

FIG. 37



Alkes, THP, 0°C 96%

(MeO)MeNH-HCI

APPROVED O.G. FIG.

BY CLASS SUB

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BY DRAFTSMAN

•			33/48	0		و الدائد
	K-Selectride	toluene-THF -95 °C 64%		TBSO,, CHO	TBSO 0 0	29
	TBSO	=0 49			0 ₃ CH ₂ Cl ₂ 84%	
119.70	OTMS 63 eq TiCl , CH 2Cl 2, -78 °C	ii) Cl ₃ CO ₂ H, CH ₂ Cl ₂ , 0 °C 56%		TBSO,	TBS0 0 0	99
	CHO i) 1 eq TiCl.	ii) Cl ₃ CO ₂ H,			TBS-Cl, imidazole DMF 95%	
	Meo N N O OTBS	(-)-27	·	HO		65

FIG. 39

(+)-BTBSO MeZnCl Pd(0) THF, -78 °C Cl4PPh3 **TBS**0 (-)-18

TBS0

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. FIG.	SUBCLASS	293
0.G. F	CLASS	bhs
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	OHC PMBO OTBS OTBS SO 72 OPMB	35/48 HIO OTHS HO	PMBO OTBS OTBS TBSO TBSO TSO TSO TSO TSO TSO TSO TSO TSO TSO T
FIG. 40	7, E	OTBS DDQ or EtSH, MgBr ₂	1) KN(TMS) ₂ , toluene, 0 °C 2) TBS0, CH0 TBS0 67 PPh ₃ l 67
	OTBS PMB0 C DIBAL OPMB	Br PMBO OTBS	PMB0 OTBS
	PMP (+)-39	1) TMS Br + CrCl ₂ , THF E add 6 M aq KOH, MeOH 92% (>20:1 Z/E)	1) Ph ₃ P, I ₂ , imidazole Benzene-Ether (1:1) 2) 4 eq Ph ₃ P, 0.5eq i-Pr ₂ NEt Benzene-Toluene(7:3) 12.8 Kbar, 16 days 76% (2 steps)

APPROVED O.G. FIG.

BY CLASS SUB

DRATSMAN STOP 29

BY CRA-TSMAN

	1) 75, KN(TMS) ₂ , 0 °C 2) DDQ, CH ₂ Cl ₂ -H ₂ 0 3) Cl ₃ CCONCO, CH ₂ Cl ₂ then neutral alumina 4) 46% HF, CH ₃ CN 85	PMBO OTBS
FIG. 41	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	HO O O O O O O O O O O O O O O O O O O

32

98

APPROVED O.G. FIG. BY CLASS SUBCLASS DRAFTSMAN S49 292	(0.7BS) 1) 10 eq DIBAL, CH_2CI_2 -78 °C10 °C (74%) 2) PDC, CH_2CI_2 , 4 Å MS (82%)	PMB OTBS OTBS OF THE SET OF THE S
	TBSO, CHO PMP TBSO, TBSO	Ph ₂ PCH ₂ CH=CH ₂ , t-Buli, TI(0i-Pr) ₄ ; Mel THF 58% (1.2:1 Z/E) or 1) TMS Br CrCl ₂ , THF Br 1) KN(TMS) ₂ , THF, 0 °C 65% (>20:1 Z/E)
	1) KN tol (+)-49 PPh ₃ l	OHC PMBO OTBS TBSO TBSO TRSO TRS

APPROVED O.G. FIG.

BY DRAFTSMAN

OTBS	38/48
HO PMB0 OTBS DIBAL-H CH ₂ Cl ₂ , 0 °C (-)-88 (89-95%)	[0] AMO
PMP OTBS OTBS (+)-87 OTF	
Dyr, 100 °C (+)-40 OH (88-93%)	

83

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b) Ti(0i-Pr)4, THF, -78 -->

OTBS

PMB0

90

a) Ph₂PCH₂CH=CH₂, t-BuLi,

c) Mel (7 equiv) 0 °C --> 24 °C (61-76%; 8:1 to 11:1 ds)

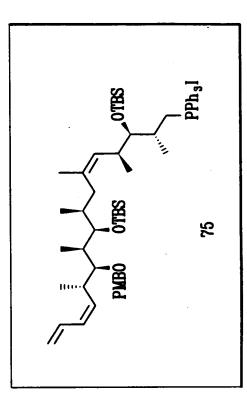
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a. FIG.	SUBCLASS	293
0.G. F	CLASS	Sy.
АРРЯОУЕВ	BY	GRAFTSMAN

39/48

HO

74

OTBS



1) PPh₃, I₂, Imid. (PhH/Et₂0)

2) PPh₃, Hunig's base (PhH/Tol.) 12.8 Kbar (7-14 days) 75-82% (2 steps)

	OTBS	40/48	
APPROVED O.G. FIG. BY CLASS SUBCLASS CRAFTSMAN 549 293	PMB0 0TBS mixture (8:1 - 12:1) TBS0,	98	HO OTBS Omer TBSO
	67 °C>-10 °C)	alt	H0 One isomer
	i) NaHMDS (0.95 eq.), -20>0 °C ii) TBSO, TBSO, (-25	59-69%, ds 15-24:1 85-95% based on s	
	OTBS		of 58

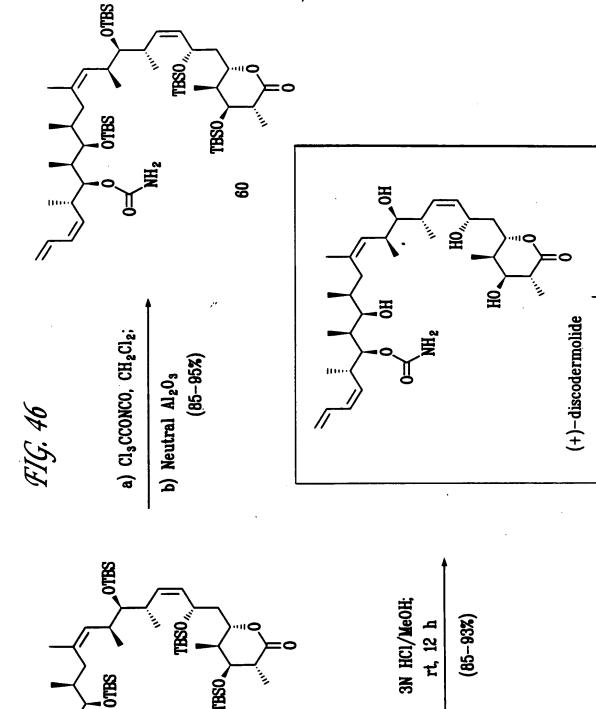
OTBS

PMB0

72

DDQ, CH2Cl2, H2O

92–96% based on starting purity of 58 (+)-29

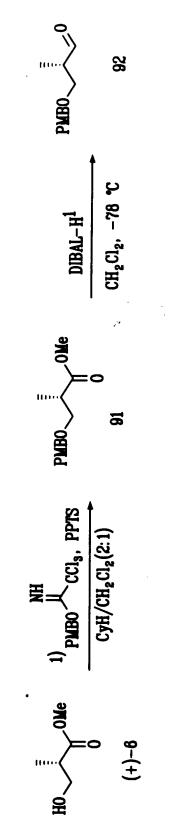


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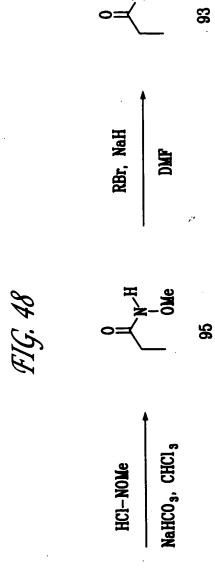
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FIG. 47



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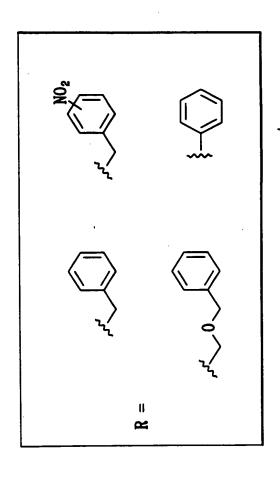
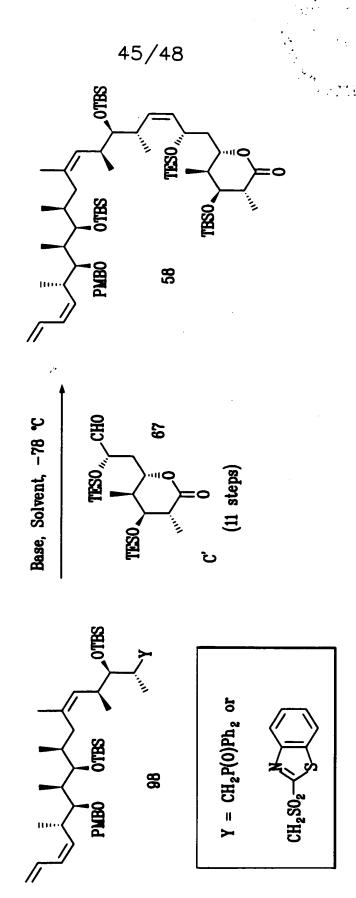


FIG. 50



APPROVED O.G. FIG.
BY CLASS SUBCLASS
ORAFTSMAN S49 29 2

1201 MgBr Cul OTr	OPMB OTBS 1202 1202	HO 00	NH ₂ HO, HO, 1205
Et ₃ N, CH ₂ Cl ₂	atecholborane I ₂ Hunig's Base	OTES	TBSO, CH ₂ CI CO)NCO CH ₂ CI ₂ , Al ₃ O ₂ 3. 3. N. HCI, MeOH
OPMB OTBS 1200 1200 OThr	H OTBS 3.	/	TBS01204
HG, 51	OPMB OTBS	NaHMDS, THF	TBS0

APPROVED O.G. FIG.

BY CLASS SUBCLASS
THATERMAN 547 2.9 2

OPMB OTBS Lialh4. Et.20 OTr	OPMB OTBS 1206 1206 1206	HO HO O	NH ₂ HO,
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$		OTBS	1. DDQ, H ₂ O, CH ₂ Cl ₂ 2. Cl ₃ CC(0)NC0 CH ₂ Cl ₂ , Al ₃ O ₂ 3. 3 N HCl, MeOH
H OTTO	 chlorocatecholborane PPh₃, I₂ PPh₃, Hunig's Base 	OPMB OTBS	TBS0, TBS0, 1208
FIG. 52 OPMB OTBS	OPMB OTBS 1207 OPMB OFBS PPh ₃ I	Na.HMDS, THF 0 TBSO, 11	TBSO

48/48

1211

TBSO,